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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,992	05/03/2001	Wilfried Lubisch	49500	7169

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WOOD, PHILLIPS, KATZ, CLARK & MORTIMER
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EXAMINER	
STOCKTON, LAURA LYNNE	
ART UNIT	**PAPER NUMBER**
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/830,992	LUBISCH ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 8, 2004 and April 12, 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-26 are pending in the application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 8, 2004 has been entered.

Election/Restrictions

During a telephone conversation with Herbert B. Keil on June 29, 2001, a provisional election was made

with traverse to prosecute the invention of Group I {products and methods of claims 1-26}.

Rejections made in the previous Office Action which do not appear below have been overcome. Therefore, arguments pertaining to these rejections will not be addressed.

It is noted that the changes in the Amendment filed April 12, 2007 are not according to the last entered amendment of June 18, 2003. However, since the last Office Action was dated September 10, 2003, the claimed invention has been re-searched and re-evaluated based on the disclosure in the specification, as originally filed, and the originally filed claims. The following rejections are now applicable.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-13, 15, 23 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating stroke, epilepsy, microinfarct and diabetes mellitus, does not reasonably provide enablement for treating any and every disorder in which pathologically elevated PARP activities occur. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets

the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

Applicant is claiming methods for treating a disorder in which pathologically elevated PARP activities occur by administering a compound of formula (I). See, for example, instant claims 11, 15 and 23. From the reading of the specification, it appears that Applicant is asserting that the embraced compounds, because of their mode action which involves the PARP inhibition, would be useful for treating numerous

diseases and disorders such as all neurodegenerative diseases, Alzheimer's disease, Huntington's disease, tumor metastasis, etc.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that cancer therapy, for example, remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known (see Golub et al., Science, Vol. 286, October 15, 1999, pages 531-537) that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, to maximize efficacy and minimize toxicity. Cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses

to therapy (Golub et al., Science, Vol. 286, October 15, 1999, pages 531-537). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

That a single class of compounds can be used to treat all diseases embraced by the claims is an incredible finding for which Applicant has not provided supporting evidence. Applicant has not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating all conditions by administering the instant claimed compounds.

The quantity of experimentation needed

The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities for each of the diseases and disorders instantly claimed. The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to testing all diseases generically embraced in the claim language, and when faced with the unpredictability of the pharmaceutical art. Thus, factors such as "sufficient working examples", "the level of skill in the art" and predictability, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

The level of the skill in the art

Even though the level of skill in the pharmaceutical art is very high, based on the

unpredictable nature of the invention and state of the prior art and lack of guidance and direction, one skilled in the art could not use the claimed invention without undue experimentation.

Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No support in the specification or the original filed claims can be found for a number of changes that Applicant is/has added to the claims. See, for example, the following list.

In claim 1, there is no support for R^2 representing $-NR^{22}R^{23}$. However, support is found in originally filed claim 3 for R^2 representing $NR^{21}R^{22}$.

In claim 1, there is no support for the entire definition of variable R^{23}. See original filed claims 1-3 and the original filed specification on page 4, line 24 which states that R^{23} represents hydrogen, C_{1-4} alkyl or phenyl.

In claims 1 and 2, there is no support for R^3 representing $-O-(CH_2)_o(CHR^{31})_m-(CH_2)-G$. However, support is found on page 8 of the originally filed specification for R^3 representing $-O-(CH_2)_o(CHR^{31})_m-(CH_2)_n-R^5$.

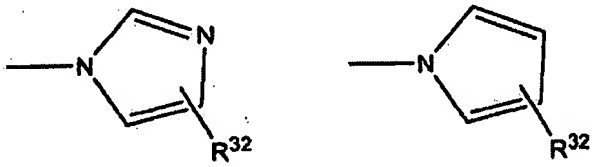
In claim 1, there is no support for the entire definition of variable K (reproduced below).

K is phenyl, $NR^{k1}R^{k2}$ where R^{k1} and ^{Rk2} are as defined for R^{41} and R^{42} respectively, NH-C_1-C_4-alkylphenyl, pyrrolidine, piperidine, 1, 2, 5, 6-tetrahydropyridine, morpholine, trihydroazepine, piperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, or homopiperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, and C_4-alkylphenyl, pyrrolidine, piperidine, 1,2, 5, 6-tetrahydropyridine, morpholine, trihydroazepine, piperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, or homopiperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, and

See originally filed claim 1 or the originally filed specification on page 7, lines 5-11 (reproduced below).

> **K is phenyl which may carry at most two radicals R, is $NR^{k1}R^{k2}$ (where R^{k1} and R^{k2} are as defined for R^{41} and R^{42} respectively), NH-C_1-C_4-alkylphenyl, pyrrolidine, piperidine, 1,2,5,6-tetrahydropyridine, morpholine, trihydroazepine, piperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, and homopiperazine, which may also be substituted by an alkyl radical C_1-C_6-alkyl, and**

In claims 1 and 2, there is no support for R^3 representing a R^{32} substituted imidazole ring or a R^{32} substituted pyrrole ring found in claims 1 and 3



However, there is support for R^3 representing a representing a $\mathbf{R^{31}}$ substituted imidazole ring or a $\mathbf{R^{31}}$ substituted pyrrole ring (see the instant specification on page 10, lines 35-40).

In claim 3, there is no support for R^{32} representing $-(CH_2)_o-(CHR^{31})_m-(CH_2)_n-G$. However, there is support for R^{31} representing $-(CH_2)_o-(CHR^{32})_m-(CH_2)_n-R^5$. See originally filed claim 3 and the originally filed specification on page 10, line 43.

In claim 7, there is no support for either $-(CH_2)_w-F$ or $-(CH_2)_p-G$ defining R^{31}. However, there is support for R^{31} representing $-(CH_2)_p-R^5$. See originally filed claim 7 or the originally filed specification on page 12, lines 5-15 and 26-35.

Applicant did not show where {page number(s) and line number(s)} persuasive support could be found in the originally filed specification or the originally filed claims. Applicant is strongly encouraged to define the variables {i.e., R^1, R^2, R^3} exactly as found in the originally filed specification or the originally filed claims. The switching of variables in substituents {i.e., using R^{32} instead of R^{31} as discussed above}, and their changing their definitions, as

Applicant has repeatedly done in the past, becomes a quagmire when trying to determine if the instant claimed invention has proper written description as originally filed. Applicants should specifically point out the support for any amendments. See M.P.E.P. §§ 714.02 and 2163.06. Therefore, the claims lack written description as such.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims continue to be replete with a multitude of errors.

Claim 1 does not conform to M.P.E.P. 608.01(m) since each claim must end with a period and no other periods may be used elsewhere in the claims except for abbreviations {e.g., see under the definitions of E, R^{51} and R^{53}}.

In claim 1, under the definition of R^3, the n subscript is missing in the formula $-O-(CH_2)_o(CHR^{31})_m-(CH_2)-G$ (see originally filed claim 2).

In claim 1, under the definition of R^3, "$-D-(F^1)_p-(E)_q,-(F^2)_r,-G$" should be changed to "$-D-(F^1)_p-(E)_q-(F^2)_r-G$".

In claim 1, under the definition of R^3, "$-E-(D)_u-(F^2)_s-(G)_v$" should be changed to "$-E-(D)_u-(F^2)_s-(G)_v$".

The R^{24} and R^{32} variables are not defined in independent claim 1.

In claim 1, under the definition of E, "isoxazole" and "piperidine" are misspelled.

In claim 1, under the definition of F^1, the comma after "it" should be deleted.

In claim 1, under the definition of u, "or I" should be changed to "or 1".

In claim 1, under the definition of R^{51}, it is unclear what is meant by "(CH_2),-K".

In claim 1, under the definition of R^{53}, "C_1-C_4 alkylarnino" should be changed to "C_1-C_4 alkylamino".

In claim 1, under the definition of K, the expression "an alkyl radical C_1-C_6-alkyl", all occurrences, is confusing.

In claim 1, under the definition of R^7, "C1-C_6-alkyl" should be changed to "C_1-C_6-alkyl".

In claim 1, under the definition of R^9, "alkyl" is misspelled.

In claim 1, under the definition of R^{53}, it would appear that a comma is missing in the expression "NH_2 CN, COOH".

In claim 1, under the definition of R^{53}, "$COOC_1$,-C_4-alkyl" should be changed to "$COOC_1$-C_4-alkyl".

In claims 1 and 2, under the definition of R^4, "branched and unbranched" should be changed to "branched or unbranched". Also see, all occurrences, in variables R^1, R^{51}, R^{52}, etc. and other claims for same.

In claim 2, under the definition of R^2, "branched and unbranched" should be changed to "branched or unbranched".

In claims 2 and 3, under the definition of R^2, an "or" should be added before OR^{21}.

In claim 2, under the definition of R^4, an "or" should be added before OR^{41}.

In claim 2, under the definition of R^4, OR^{41} lacks antecedent basis from claim 1.

In claims 2 and 3, an "or" should be added before the last substituent listed under the definition of R^{52} (also the possible substitutable substituents).

In claim 2, under the definition of R^{52} and R^{53}, a space is needed before "CCl_3".

In claim 3, under the definition of variable G, an "or" should be added before the last substituent listed.

Claim 7 lacks antecedent basis from claim 1 because of the imidazole and pyrrole ring being substituted by R^{31}.

In claim 7, the R^{31} variable definition lacks antecedent basis from claim 1.

In claim 7, p representing 2 lacks antecedent basis from claim 1.

In claim 7, under the definition of R^{52}, the alkyl being optionally substituted lacks antecedent basis from claim 1.

In claim 7, before definition (iii), one of the two "and" should be deleted.

In claim 9, both the definition of R^5 and R^{52} lacks antecedent basis from claim 1.

In claim 23, Applicant has added an "I" but this amendment makes the claim unclear.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4-6 and 9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 10 of copending Application No. 11/536,994. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed invention is generically claimed in the copending application. See, for example, the first compound listed in independent claim 10 of the copending application.

The indiscriminate selection of "some" among "many" is *prima facie* obvious, *In re Lemin*, 141 USPQ 814 (1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., treating sepsis).

One skilled in the art would thus be motivated to prepare products embraced by the copending application to arrive at the instant claimed products with the

expectation of obtaining additional beneficial products which would be useful in treating, for example, sepsis. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-6 and 8-26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 7-22 of U.S. Patent No. 6,696,437. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed invention is generically claimed in the patent.

The indiscriminate selection of "some" among "many" is *prima facie* obvious, *In re Lemin*, 141 USPQ 814 (1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., diabetes mellitus).

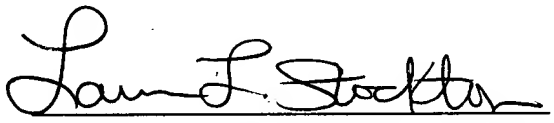
One skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful in treating, for example, diabetes mellitus. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached

on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.



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July 9, 2007